

Amendments to the Specification:

Please amend the paragraph which follows the "Related Applications" heading, page 1, lines 4-8 as shown below.

This application is a divisional of patent application serial no. 08/468,719, filed June 6, 1995, which is a divisional continuation of patent application serial no. 08/108,591, now U.S. Patent No. 6,395,474, filed November 22, 1993, which is a continuation-in-part of the following Danish Patent Applications: No. 986/91, filed May 24, 1991, No. 987/91, filed May 24, 1991, and No. 510/92, filed April 15, 1992. The entire disclosure of each application is incorporated herein by reference.

Please amend the paragraph at page 14, lines 1-8 as follows.

- FIGS. 11A and 11B show binding of AcrT₁₀-Lys to dA₁₀ (SEQ ID NO: 1) 5'-³²P-labeled oligonucleotide (1) (5'-GATCCA₁₀ G) (SEQ ID NO: 2) was incubated in the absence or presence of Acr-T₁₀-LysNH₂ and in the absence or presence of oligonucleotide (2) (5'-GATCCT₁₀G) (SEQ ID NO: 3) and the samples were analyzed by polyacrylamide gel electrophoresis (PAGE) and autoradiography under "native conditions" (FIG. 11a) or under "denaturing conditions" (FIG. 11b).

Please amend the paragraph at page 14, lines 9-18 as shown below.

FIGS. 12A-C show chemical, photochemical and enzymatic probing of dsDNA-Acr-T₁₀-LysNH₂ complex. Complexes between Acr-T₁₀-LysNH₂ and a ³²P-endlabeled DNA fragment containing a dA₁₀ (SEQ ID NO: 1)/dT₁₀ (SEQ ID NO: 4) target sequence were probed by affinity photocleavage (FIG. 12a, lanes 1-3; FIG. 12b, lanes 1-3), photofootprinting (FIG. 12a, lanes 5-6), potassium permanganate probing (FIG. 12b, lanes 4-6) or probing by staphylococcus nuclease (FIG. 12b, lanes 8-10) or by nuclease S.sub.1 (FIG. 12c). Either the A-strand (FIG. 12a) or the T-strand (FIGS. 12b,c) was probed.

Please amend the paragraph at page 15, lines 12-14 as follows.

FIG. 24 shows a PAGE autoradiograph demonstrating that ^{125}I -labeled PNA-T₁₀ binds to a complementary dA₁₀ (SEQ ID NO: 1) oligonucleotide.

Please amend the paragraph at page 19, lines 8-17 as shown below.

Using the S₁-nuclease probing technique, the discrimination of binding of the T₁₀ (SEQ ID NO: 4), T₅CT₄ (T₉C) (SEQ ID NO: 5) & T₂CT₂CT₄ (T₈C₂) (SEQ ID NO: 6) PNA to the recognition sequences A₁₀ (SEQ ID NO: 1), A₅GA₄ (A₉G) (SEQ ID NO: 7) & A₂GA₄GA₄ (A₈G₂) (SEQ ID NO: 8) cloned into the *Bam*HI, *Sall* or *Pst*I site of the plasmid pUC19 was analyzed. The results (FIG. 20) show that the three PNAs bind to their respective recognition sequences with the following relative efficiencies: PNA-T₁₀: A₁₀ > A₉G >> A₈G₂, PNA-T₉C: A₉G > A₁₀ ≈ A₈G₂, PNA-T₈C₂: A₈G ≥ A₉G >> A₁₀. Thus at 37 °C. one mismatch out of ten gives reduced efficiency (5-10 times estimated) whereas two mismatches are not accepted.

Please amend the paragraph at page 19, lines 24-30 as follows.

Complexes between PNA-T_n and 32P-dsDNA (A₁₀ (SEQUENCE ID NO: 1) / T₁₀ (Sequence ID NO: 4)) target were formed (60 min, 37°C). The complexes were then incubated at the desired temperature in the presence of excess oligo-dA₁₀ for 10 min, cooled to RT and probed with KMnO₄. The results (Figure 22) show that the thermal stability of the PNA-dsDNA complexes mirror that of the PNA oligonucleotide complexes in terms of "T_m".

Please amend the paragraph at page 19, line 33 to page 20, line 5 as follows.

The plasmid construct, pT₁₀, contains a dA₁₀ (SEQ ID NO: 1) / dT₁₀ (SEQ ID NO: 4) tract cloned into the *Bam*HI site in pUC₁₉. Thus, cleavage of pT₁₀ with *Bam*HI and *Pvu*II results in two small DNA fragments of 211 and 111 bp, respectively. In the presence of PNA-T₁₀, a 336 bp fragment is obtained corresponding to cleavage only by *Pvu*II (Figure 23).

Thus cleavage by *Bam*HI is inhibited by PNA bound proximal to the restriction enzyme site. The results also show that the PNA-dsDNA complex can be formed in 100% yield. Similar results were obtained using the pT₈C₂ plasmid and PNA-T₈C₂.

Please amend the paragraph at page 20, lines 8-12 as shown below.

A Tyr-PNA-T₁₀-Lys-NH₂ was labeled with ¹²⁵I using Na¹²⁵I and chloramine-T and purified by HPLC. The ¹²⁵I-PNA-T₁₀ was shown to bind to oligo-dA₁₀ (SEQ ID NO: 1) by PAGE and autoradiography (Figure 24). The binding could be competed by excess denatured calf thymus DNA.

Please amend the paragraph at page 20, lines 13-19 as shown below.

The sequence-specific recognition of dsDNA is illustrated by the binding of a PNA, consisting of 10 thymine substituted 2-aminoethylglycyl units, which C-terminates in a lysine amide and N-terminates in a complex 9-aminoacridine ligand (9-Acr¹-(Taeg)₁₀-Lys-NH₂, Figure 11a, 11b) to a dA₁₀ (SEQ ID NO: 1) / dT₁₀ (SEQ ID NO: 4) target sequence. The target is contained in a 248 bp ³²P-end-labelled DNA-fragment.

Please amend the paragraph at page 20, lines 20-27 as follows.

Strand displacement was ascertained by the following type of experiments:

1) The 9-Acr¹ ligand (Figure 5), which is equipped with a 4-nitrobenzamido group to ensures cleavage of DNA upon irradiation, is expected only to cleave DNA in close proximity to its binding site. Upon irradiation of the PNA with the above 248 bp DNA fragment, selective cleavage at the dA₁₀ (SEQ ID NO: 1) / dT₁₀ (SEQ ID NO: 4) sequence is observed (Figure 3a).

Please amend the paragraph at page 20, line 36 to page 21, line 2 as follows.

3) In a similar type of experiment, the DNA-cleaving enzyme micrococcus nuclease, which is also hindered in its action by most DNA-binding reagents, showed increased cleavage at the T₁₀-target (SEQ ID NO:4, Figure 3c).

Please amend the paragraph at page 21, lines 3-8 as shown below.

4) In yet another type of experiment, the well-known high susceptibility of single strand thymine ligands (as opposed to double strand thymine ligands) towards potassium permanganate oxidation was employed. Oxidation of the 248 bp in the presence of the reagent showed only oxidation of the T₁₀-strand (SEQ ID NO:4) of the target (Figure 3b).

Please amend the paragraph at page 21, lines 9-11 as follows.

5) In a similar type of demonstration, the single strand specificity of S₁ nuclease clearly showed that only the T₁₀-strand (SEQ ID NO: 4) of the target was attacked (Figure 3d).

Please amend the paragraph at page 21, lines 12-24 as shown below.

The very efficient binding of (Taeg)₁₀, (Taeg)₁₀-Lys-NH₂ and Acr¹-(Taeg)₁₀-Lys-NH₂ (Figures 11a, 11b) to the corresponding dA₁₀ was furthermore illustrated in two ways:

1. Ligand-oligonucleotide complexes will migrate slower than the naked oligonucleotide upon electrophoresis in polyacrylamide gels. Consequently, such experiments were performed with Acr¹-(Taeg)₁₀-Lys-NH₂ and ³²P-end-labelled dA₁₀ (SEQ ID NO: 1). This showed retarded migration under conditions where a normal dA₁₀ (SEQ ID NO: 1) / dT₁₀ (SEQ ID NO: 4) duplex is stable, as well as under conditions where such a duplex is unstable (denaturing gel). A control experiment was performed with a mixture of Acr¹-(Taeg)₁₀-Lys-NH₂ and ³²P-end-labelled dT₁₀ (SEQ ID NO: 4) which showed no retardation under the above conditions.

Please amend the paragraph at page 22, lines 12-26 as follows.

List of oligodeoxyribonucleotides:

1. 5'-AAA-AAA-AA (SEQ ID NO: 1)
2. 5'-AAA-AAA-AAA-A (SEQ ID NO: 4)
3. 5'-TTT-TTT-TTT-T (SEQ ID NO: 9)
4. 5'-AAA-AAG-AAA-A (SEQ ID NO: 10)
5. 5'-AAG-AAG-AAA-A (SEQ ID NO: 11)
6. 5'-AAA-AGA-AAA-A (SEQ ID NO: 12)
7. 5'-AAA-AGA-AGA-A (SEQ ID NO: 13)
8. 5'-TTT-TCT-TTT-T (SEQ ID NO: 14)
9. 5'-TTT-TCT-TCT-T (SEQ ID NO: 15)
10. 5'-TTT-TTC-TTT-T (SEQ ID NO: 16)
11. 5'-TTT-TTC-TTC-T (SEQ ID NO: 17)
12. 5'-TTC-TTC-TTT-T (SEQ ID NO: 18)
13. 5'-TTT-TTT-TTT-TTT-TTT (SEQ ID NO: 19)
14. 5'-AAA-AAA-AAA-AAA-AAA (SEQ ID NO: 19)

Please amend the paragraph at page 68, lines 16-30 as shown below.

Acr¹-(Taeg)₁₀-Lys (100 ng) was incubated for 15 min at room temperature with 50 cps 5'-[³²P]-end-labeled ~~labelled~~ oligonucleotide [d(GATCCA₁₀G) (SEQ ID NO:2)] in 20 µl TE buffer (10 mM Tris-HCl, 1 mM EDTA, pH 7.4). The sample was cooled in ice (15 min) and analyzed by gel electrophoresis in polyacrylamide (PAGE). To 10 µl of the sample was added 2 µl 50% glycerol, 5 TBE (TBE = 90 mM Tris-borate, 1 mM EDTA, pH 8.3), and the sample was analysed by PAGE (15% acrylamide, 0.5% bisacrylamide) in TBE buffer at 4°C. A 10 µl portion of the sample was lyophilized and redissolved in 10 µl 80% formamide, 1 TBE, heated to 90°C (5 min), and analyzed by urea/PAGE (15% acrylamide, 0.5% bisacrylamide, 7 M urea) in TBE. [³²P]-containing DNA bands were visualized by autoradiography using intensifying screens and Agfa Curix RPI X-ray films exposed at -80°C for 2 h.

Please amend the paragraph at page 69, lines 3-24 as follows.

A dA₁₀ (SEQ ID NO: 1) -dT₁₀ (SEQ ID NO: 4) target sequence contained within a plasmid DNA sequence was constructed by cloning of two oligonucleotides (d(GATCCA₁₀G) (SEQ ID NO: 2) + d(GATCCT₁₀G) (SEQ ID NO: 3)) into the *Bam*HI restriction enzyme site of pUC19 using the *Eschericia coli JM101* strain by standard techniques (Maniatis et al., 1986). The desired plasmid (designated pT₁₀) was isolated from one of the resulting clones and purified by the alkaline extraction procedure and CsCl centrifugation (Maniatis et al., 1986). A 3'-[³²P]-end-labelled DNA fragment of 248 bp containing the dA₁₀ (SEQ ID NO: 1) /dT₁₀ (SEQ ID NO: 4) target sequence was obtained by cleaving the pT₁₀ DNA with restriction enzymes *Eco*RI and *Pvu*II, ~~labelling~~ labeling of the cleaved DNA with α[³²P]-dATP (4000 Ci/mmol, Amersham) using the Klenow fragment of *E. coli* DNA polymerase (Boehringer Mannheim), and purifying the 248 bp DNA fragment by PAGE (5% acrylamide, 0.06% bisacrylamide, TBE buffer). This DNA fragment was obtained with [³²P]-~~endlabelling~~ endlabeling at the 5'-end by treating the *Eco*RI-cleaved pT₁₀ plasmid with bacterial alkaline phosphatase (Boehringer Mannheim), purifying the plasmid DNA by gel electrophoresis in low melting agarose, and ~~labelling~~ labeling with γ[³²P] ATP and polynucleotide kinase. Following treatment with *Pvu*II, the 248 bp DNA fragment was purified as above.

Please amend the paragraph at page 96, lines 8-30 as shown below.

Hybridization experiments with the PNA-oligomer H-T4C2TCTC-LysNH₂ were performed as follows:

Row	Hybridized With	<u>SEQ ID</u> <u>NO:</u>	pH	Tm	§
1	5'-(dA) ₄ (dG) ₂ (dA)(dG)(dA)(dG)	<u>20</u>	7.2	55.5	2:1
2	5'-(dA) ₄ (dG) ₂ (dA)(dG)(dA)(dG)	<u>20</u>	9.0	26.0	2:1
3	5'-(dA) ₄ (dG) ₂ (dA)(dG)(dA)(dG)	<u>20</u>	5.0	88.5	2:1
4	5'-(dG)(dA)(dG)(dA)(dG) ₂ (dA) ₄	<u>21</u>	7.2	38.0	2:1
5	5'-(dG)(dA)(dG)(dA)(dG) ₂ (dA) ₄	<u>21</u>	9.0	31.5	-

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6	5'-(dG)(dA)(dG)(dA)(dG) ₂ (dA) ₄	<u>21</u>	5.0	52.5	-
7	5'-(dA) ₄ (dG)(dT)(dA)(dG)(dA)(dG)	<u>22</u>	7.2	39.0	-
8	5'-(dA) ₄ (dG)(dT)(dA)(dG)(dA)(dG)	<u>22</u>	9.0	<20	-
9	5'-(dA) ₄ (dG)(dT)(dA)(dG)(dA)(dG)	<u>22</u>	5.0	51.5	-
10	5'-(dA) ₄ (dG) ₂ (dT)(dG)(dA)(dG)	<u>23</u>	7.2	31.5	-
11	5'-(dA) ₄ (dG) ₂ (dT)(dG)(dA)(dG)	<u>23</u>	5.0	50.5	-
12	5'-(dG)(dA)(dG)(dA)dT(dG)(dA) ₄	<u>24</u>	7.2	24.5	-
13	5'-(dG)(dA)(dG)(dA)dT(dG)(dA) ₄	<u>24</u>	9.0	<20	-
14	5'-(dG)(dA)(dG)(dA)dT(dG)(dA) ₄	<u>24</u>	5.0	57.0	-
15	5'-(dG)(dA)(dG)(dT)(dG) ₂ (dA) ₄	<u>25</u>	7.2	25.0	-
16	5'-(dG)(dA)(dG)(dT)(dG) ₂ (dA) ₄	<u>25</u>	5.0	39.5	-
				52.0	

§ = stoichiometry determined by UV-mixing curves
- = not determined

Please amend the paragraph at page 97, lines 18 to 27 as follows.

The results of hybridization experiments with H-T₅GT₄-LysNH₂ to were performed as follows:

Row	Deoxyoligonucleotide	<u>SEQ ID NO</u>	T _m
1	5'-(dA) ₅ (dA)(dA) ₄ -3'	<u>1</u>	55.0
2	5'-(dA) ₅ (dG)(dA) ₄ -3'	<u>9</u>	47.0
3	5'-(dA) ₅ (dG)(dA) ₄ -3'	<u>9</u>	56.5
4	5'-(dA) ₅ (dT)(dA) ₄ -3'	<u>26</u>	46.5
5	5'-(dA) ₄ (dG)(dA) ₅ -3'	<u>11</u>	48.5
6	5'-(dA) ₄ (dC)(dA) ₅ -3'	<u>27</u>	55.5
7	5'-(dA) ₄ (dT)(dA) ₅ -3'	<u>28</u>	47.0

Please amend the paragraph at page 98, lines 15-24 as shown below.

Hybridization data for a PNA-oligomer with a single unit with an extended backbone (the β -alanine modification) is as follows:

PNA	DNA	<u>SEQ ID NO</u>	T _m
H-T ₁₀ -LysNH ₂ H-T ₁₀ -LysNH ₂	(dA) ₁₀	<u>1</u>	73°C
H-T ₄ (β T)T ₅ -LysNH ₂	(dA) ₁₀	<u>1</u>	57°C
H-T ₄ (β T)T ₅ -LysNH ₂	(dA) ₄ (dG)(dA) ₅	<u>11</u>	47°C
H-T ₄ (β T)T ₅ -LysNH ₂	(dA) ₄ (dT)(dA) ₅	<u>28</u>	49°C
H-T ₄ (β T)T ₅ -LysNH ₂	(dA) ₄ (dT)(dA) ₅	<u>28</u>	47°C

Please amend the table at page 99, lines 16-26 as follows.

PNA	DNA	<u>SEQ ID NO</u>	T _m
H-T ₁₀ -LysNH ₂	(dA) ₁₀	<u>1</u>	73°C
H-T ₄ (Ac)T ₅ -LysNH ₂	(dA) ₁₀	<u>1</u>	49°C
H-T ₄ (Ac)T ₅ -LysNH ₂	(dA) ₄ (dG)(dA) ₅	<u>11</u>	37°C
H-T ₄ (Ac)T ₅ -LysNH ₂	(dA) ₄ (dC)(dA) ₅	<u>27</u>	41°C
H-T ₄ (Ac)T ₅ -LysNH ₂	(dA) ₄ (dT)(dA) ₅	<u>28</u>	41°C
H-T ₄ (Ac)T ₅ -LysNH ₂	(dA) ₅ (dG)(dA) ₄	<u>9</u>	36°C
H-T ₄ (Ac)T ₅ -LysNH ₂	(dA) ₅ (dC)(dA) ₄	<u>29</u>	40°C
H-T ₄ (Ac)T ₅ -LysNH ₂	(dA) ₅ (dT)(dA) ₄	<u>26</u>	40°C

Please amend the paragraph at page 100, lines 2-3 as follows.

Binding of PNAs-T₁₀/T₉C/T₈C₂ to double stranded DNA targets A₁₀ (SEQ ID NO: 1) / A₉G (SEQ ID NO: 30) / A₈G₂ (SEQ ID NO: 31) (Figure 20).

A mixture of 200 cps ³²P-labeled *EcoRI*-*PvuII* fragment (the large fragment labeled at the 3'-end of the *EcoRI* site) of the indicated plasmid, 0.5 μ g carrier calf thymus DNA, and 300 ng PNA in 100 μ l buffer (200 mM NaCl, 50 mM Na-acetate, pH 4.5, 1 mM ZnSO₄) was incubated at 37°C for 120 min. A 50 unit portion of nuclease S₁ was added and incubated at 20°C for 5 min. The reaction was stopped by addition of 3 μ l 0.5 M EDTA and the DNA was precipitated by addition of 250 μ l 2% potassium acetate in ethanol. The DNA was

analyzed by electrophoresis in 10% polyacrylamide sequencing gels and the radiolabeled DNA bands visualized by autoradiography.

Please amend the paragraph at page 100, lines 15-23 as shown below.

The target plasmids were prepared by cloning of the appropriate oligonucleotides into pUC19. Target A₁₀: oligonucleotides GATCCA₁₀G (SEQ ID NO: 2) & GATCCT₁₀G (SEQ ID NO: 3) cloned into the *Bam*HI site (plasmid designated pT₁₀). Target A₅GA₄ (SEQ ID NO: 27): oligonucleotides TCGACT₄CT₅G (SEQ ID NO: 34) & TCGACA₅GA₄G (SEQ ID NO: 35) cloned into the *Sal*I site (plasmid pT9C). Target A₂GA₂GA₄: oligonucleotides GA₂GA₂GA₄TGCA & GT₄CT₂CT₂CTGCA into the *Pst*I site (plasmid pT8C2). The positions of the targets in the gel are indicated by bars to the left. A/G is an A+G sequence ladder of target P10.

Please amend the paragraph at page 101, lines 20-28 as follows.

A mixture of 200 cps ³²P-pT₁₀ fragment, 0.5 µg calf thymus DNA and 300 ng of the desired PNA (either T₁₀-LysNH₂, T₈-LysNH₂ or T₆-LysNH₂) was incubated in 100 µl 200 mM NaCl, 50 mM Na-acetate, pH 4.5, 1 mM ZnSO₄ for 60 min at 37°C. A 2 µg portion of oligonucleotide GATCCA₁₀G (SEQ ID NO: 2) was added and each sample was heated for 10 min at the temperature indicated, cooled in ice for 10 min and warmed to 20°C. A 50 U portion of S₁ nuclease was added and the samples treated and analyzed and the results quantified.

Please amend the paragraph spanning page 101, line 32 to page 102, line 14 as shown below.

A mixture of 100 ng plasmid DNA (cleaved with restriction enzyme *Pvu*II (see below) and 100 ng of PNA in 15 µl 10 mM Tris-HCl, 1 mM EDTA, pH 7.4 was incubated at 37°C for 60 min. Subsequently, 4 µl 5 × concentrated buffer (0.2 M Tris-HCl (pH 8.0), 40 mM MgCl₂, 10 mM spermidine, 125 mM NaCl) were mixed with 1 µl NTP-mix (10 mM

ATP, 10 mM CTP, 10 mM GTP, 1 mM UTP, 0.1 $\mu\text{Ci}/\mu\text{l}$ ^{32}P -UTP, 5 mM DTT, 2 $\mu\text{g}/\text{ml}$ tRNA, 1 $\mu\text{g}/\text{ml}$ heparin) and 3 units RNA polymerase. Incubation was continued for 10 min at 37°C. The RNA was then precipitated by addition of 60 μl 2% potassium acetate in 96% ethanol at -20°C and analyzed by electrophoresis in 8% polyacrylamide sequencing gels. RNA transcripts were visualized by autoradiography. The following plasmids were used: pT8C2-KS/pA8G2-KS: oligonucleotides GA₂GA₂GA₄GTGAC (SEQ ID NO: 36) & GT₄CT₂CT₂CTGCA (SEQ ID NO: 35) cloned into the *Pst*I site of pBluescript-KS+; pT10-KS/pA10-KS (both orientations of the insert were obtained). pT10UV5: oligonucleotides GATCCA₁₀G (SEQ ID NO: 2) & GATCCT₁₀G (SEQ ID NO: 3) cloned into the *Bam*HI site of a pUC18 derivative in which the lac UV5 *E. coli* promoter had been cloned into the EcoRI site (Jeppesen, et al., Nucleic Acids Res., 1988, 16, 9545).

Please amend the paragraph at page 102, lines 15-24 as follows.

Using T3-RNA polymerase, transcription elongation arrest was obtained with PNA-T₈C₂-LysNH₂ and the pA8G2-KS plasmid having the PNA recognition sequence on the template strand, but not with pT8C2-KS having the PNA recognition sequence on the non-template strand. Similar results were obtained with PNA-T₁₀-LysNH₂ and the plasmids pA10-KS and pT10-KS. (see, Figure 25) Using *E. coli* RNA polymerase and the pT10UV5 plasmid (A₁₀-sequence (SEQ ID NO 1) on the template strand) transcription elongation arrest was obtained with PNA-T₁₀-LysNH₂.

Please amend the paragraph at page 107, lines 17-25 as shown below.

The title compound hybridized with the following oligonucleotides:

Oligodeoxynucleotide	SEQ ID NO	pH	T _m (°C)
5'-AAT AGT AGT G-3'	<u>37</u>	5	31.5†
5'-ATT AGT AGT G-3'	<u>38</u>	7.2	28.5†
5'-AAT AGT AGT G-3"	<u>37</u>	9	28.0†
5'-GTG ATG ATA A-3'	<u>39</u>	7.2	30.5

5'-GTG ATG ATA A-3' 39 9 28.0

†Low hypochromicity

Please amend the table at page 111, lines 2-10 as follows.

Hybridization properties of H-[Taeg]₄-[proT]-[Taeg]₅-Lys-NH₂

Oligodeoxynucleotide	<u>SEQ ID NO</u>	Tm(°C)
5'-AAA AAA AAA A	<u>1</u>	53.5
5'-AAA AGA AAA A	<u>11</u>	44.0
5'-AAA AAG AAA A	<u>9</u>	43.5
5'-AAA ACA AAA A	<u>27</u>	46.5
5'-AAA AAC AAA A	<u>29</u>	46.5
5'-AAA ATA AAA A	<u>28</u>	46.5
5'-AAA AAT AAA A	<u>26</u>	46.0

Please amend the table at page 112, lines 2-12 as shown below.

Hybridization properties of H-T₄bCT₅-Lys-NH₂

Oligodeoxynucleotide	<u>SEQ ID NO.</u>	Tm(°C)
5'-AAA AAA AAA A	<u>1</u>	43.5
5'-AAA AGA AAA A	<u>11</u>	58.0
5'-AAA AAG AAA A	<u>9</u>	60.0
5'-AAA ACA AAA A	<u>27</u>	34.5
5'-AAA AAC AAA A	<u>29</u>	34.5
5'-AAA ATA AAA A	<u>28</u>	34.0
5'-AAA AAT AAA A	<u>26</u>	36.0

Please amend the table at page 113, lines 2-10 as shown below.

Hybridization properties of H-T₄AT₅-LysNH₂

Oligodeoxynucleotide	<u>SEQ ID NO</u>	Tm(°C)
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5'-AAA AAA AAA A	<u>1</u>	59.5
5'-AAA AGA AAA A	<u>11</u>	45.0
5'-AAA AAG AAA A	<u>9</u>	45.5
5'-AAA ACA AAA A	<u>27</u>	48.0
5'-AAA AAC AAA A	<u>29</u>	48.0
5'-AAA ATA AAA A	<u>28</u>	52.0
5'-AAA AAT AAA A	<u>26</u>	52.5

Please amend the paragraph at page 114, lines2-6 as follows.

Hybridization properties of crude (approx. 50%) H-T₄G₂TGTG-LysNH₂

Oligodeoxynucleotide	<u>SEQ ID NO</u>	T _m
5'-A ₄ C ₂ ACAC	<u>40</u>	38
5'-CACAC ₂ A ₄	<u>41</u>	55